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(54) Title: PHARMACEUTICAL FORMULATION OF OLANZAPINE

(57) Abstract: A pharmaceutical formulation comprising a homogeneous mixture of (a) olanzapine or a pharmaceutically acceptable salt thereof as an active ingredient, (b) a monosaccharide and/or oligosaccharide, (c) a polysaccharide and, optionally, further ingredients.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K9/20 A61K31/551 A61P25/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | EP 0 830 858 A (LILLY CO ELI) 25 March 1998 (1998-03-25) cited in the application page 5, line 1-51; example 3 | 1-11, 14-16 |
| E | WO 03/086361 A (DESHMUKH ABHIJIT MUKUND ; DHANORKAR VIPIN TATYASAHEB (IN); DIVI MURALI) 23 October 2003 (2003-10-23) example 7-9 example 13 | 1,8,10, 11,15,16 |

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Information on patent family members

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| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
|---|---|---------------------|----------------------------|---------------------|
| EP 0830858 | A | 25-03-1998 | AU 719788 B2 | 18-05-2000 |
| | | | AU 4423097 A | 17-04-1998 |
| | | | BR 9713215 A | 04-04-2000 |
| | | | CA 2266448 A1 | 02-04-1998 |
| | | | CN 1230883 A | 06-10-1999 |
| | | | CZ 9900988 A3 | 15-12-1999 |
| | | | EA 1610 B1 | 25-06-2001 |
| | | | EP 0830858 A1 | 25-03-1998 |
| | | | HU 9904065 A2 | 28-04-2000 |
| | | | ID 21762 A | 22-07-1999 |
| | | | JP 2001501207 T | 30-01-2001 |
| | | | KR 2000048540 A | 25-07-2000 |
| | | | NO 991405 A | 23-03-1999 |
| | | | PL 332503 A1 | 13-09-1999 |
| | | | TR 9900651 T2 | 21-07-1999 |
| | | | WO 9813027 A1 | 02-04-1998 |
| | | | US 2001020032 A1 | 06-09-2001 |
| | | | ZA 9708517 A | 23-03-1999 |
| WO 03086361 | A | 23-10-2003 | WO 03086361 A1 | 23-10-2003 |

Claims

1. A pharmaceutical formulation comprising a homogeneous mixture of (a) olanzapine or a pharmaceutically acceptable salt thereof as an active ingredient, (b) a monosaccharide and/or oligosaccharide, and (c) a polysaccharide.
2. The pharmaceutical formulation of claim 1 comprising 40 to 80 weight % of the component (b).
3. The pharmaceutical formulation of any one of claims 1 to 2 comprising 10 to 40 weight % of the polysaccharide.
4. The pharmaceutical formulation of any one of claims 1 to 3 additionally comprising (d) up to 15 weight % of a disintegrant.
5. The pharmaceutical formulation of any one of claims 1 to 4 additionally comprising (e) 5 to 20 weight % of a binder.
6. The pharmaceutical formulation of any one of claims 1 to 5 additionally comprising (f) 0.25 to 5 weight % of a lubricant.
7. The pharmaceutical formulation of any one of claims 1 to 6 additionally comprising (g) 0.1 to 0.5 weight % of a glidant.
8. The pharmaceutical formulation of any one of claims 1 to 7, wherein the component (b) is selected from the group consisting of lactose, sucrose, dextrose, sorbitol, mannitol, lactitol, and mixtures thereof.
9. The pharmaceutical formulation of claim 8, wherein the component (b) is lactose.

10. The pharmaceutical formulation of any one of claims 1 to 9, wherein the polysaccharide is selected from the group consisting of starch, cellulose, and mixtures thereof.
11. The pharmaceutical formulation of claim 10, wherein the polysaccharide is cellulose.
12. The pharmaceutical formulation of claim 11, wherein a mixture of 20 to 30 weight % of cellulose and 70 to 80 weight % of lactose is used as the components (b) and (c).
13. The pharmaceutical formulation of claim 12 comprising
70 to 90 weight % of a mixture of 20 to 30 weight % of cellulose and 70 to 80 weight % of lactose;
8 to 12 weight % of a binder;
3 to 10 weight % of a disintegrant;
0.3 to 2 weight % of a lubricant; and
0.2 to 0.4 weight % of a glidant.
14. The pharmaceutical formulation of any one of claims 1 to 13 obtainable by direct compression.
15. The pharmaceutical formulation of any one of claims 1 to 14 comprising olanzapine as the only pharmaceutically active ingredient.
16. The pharmaceutical formulation of any one of claims 1 to 15 having the form of an uncoated tablet.
17. A process for preparing a stable pharmaceutically solid oral formulation according to any one of claims 1 to 16 comprising combining (a) olanzapine or a pharmaceutically acceptable salt thereof with (b) a monosaccharide and/or oligosaccharide, (c) a polysaccharide and optionally one or more of components (d) to (g), followed by a direct compression of the mixture into tablets in the absence of any solvent.